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Ethnic Differences in Presentation and Severity of Alcoholic Liver Disease

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Abstract

Background—The frequency of alcoholic liver disease (ALD), including alcoholic steatosis, hepatitis and cirrhosis, varies significantly by ethnicity.

Methods—With the goal to assess the role of ethnicity in determining the age of onset and severity of ALD and to compare the risk factors for its progression among ethnic groups, we conducted a retrospective chart review of all patients with ALD who were admitted or were followed as outpatients at University of California Davis Medical Center between 2002 and 2010. After excluding HBsAg and HIV positive subjects, we reviewed the charts of 791 ALD patients including 130 with alcoholic fatty liver, 154 with alcoholic hepatitis, and 507 with alcoholic cirrhosis.

Results—When controlling for all variables in the model, Hispanic patients presented at significantly 4-10 years younger ages than White/Caucasian patients, in each of the three disease severity categories and the results were confirmed after excluding HCV Ab/RNA positive subjects. There were more obese Hispanic patients than White/Caucasian patients, whereas the proportion of patients with hepatitis C was significantly greater in African/American subjects with alcoholic hepatitis and the proportion of patients with diabetes mellitus was significantly lower in White/Caucasian subjects than in Hispanic subjects with cirrhosis. The proportion of subjects with severe alcoholic hepatitis was similar in Hispanic and White/Caucasian patients, but lower in African/American subjects.

Conclusion—Ethnicity is a major factor affecting the age and severity of presentation of different subtypes of ALD.

Keywords

Alcoholic; Alcoholic Liver Disease; Ethnicity; Hispanic

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Introduction

About 4.6% of Americans meet the criteria for alcohol abuse within the preceding 12 months (Hasin et al., 2007) where alcohol abuse is defined by the recurrent use of alcohol with consequent significant health, social, or legal ramifications (American Psychiatric Association., 2000). Drinking habits associated with increased risk of alcohol-related harm, or heavy drinking, are defined as consuming 15 or more standard drinks per week or 5 or more on one occasion for men, or 8 or more drinks weekly, or 4 or more on one occasion for women and people older than 65 years of age, where one drink of 14 g alcohol is found in 12 oz of beer, 5 oz of wine, or 1.5 oz of 80-proof (40%) liquor (Friedmann, 2013). These chronic alcoholic patients are at risk for developing alcoholic liver disease (ALD) which encompasses a broad spectrum of alcohol related liver injury including alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. ALD is among the most frequent liver diseases in the United States. In 2010, 15,990 patients died of its complications, which is more than all other types of liver disease combined (Chen, 2006). Furthermore, ALD is one of the top indications for transplantation in the United States (Mailey et al., 2009)

Whereas the likelihood of developing cirrhosis is much greater in chronic alcoholics than in the general population, not all alcoholics develop ALD, and the severity of ALD and liver dysfunction is not solely due to the amount and duration of alcohol ingested. Whereas the ingestion of at least 30 grams of alcohol per day over 20 years is associated with increased risk of cirrhosis, the majority of heavy drinkers will not develop cirrhosis (Bellentani et al., 1997). The age-adjusted death rate from all causes of cirrhosis in Hispanic males in the United States was 1.8 times the rate for White non-Hispanic or African/American non-Hispanic males in 2008 (Yoon, 2008). Others showed that African/American and Hispanic individuals were more likely to have a 2-fold elevation in aspartate aminotransferase (AST) levels when compared with white non-Hispanic Americans. The finding that the difference was most pronounced in the highest alcohol consumers suggested an ethnic component to the pattern of liver injury (Stewart, 2002). Data from a multicenter Veterans Affairs (VA) cooperative study showed that features of cirrhosis are more frequent in Hispanic (73%) than in non-Hispanic White/Caucasian (52%) and African/American (44%) patients with acute alcoholic hepatitis (Mendenhall et al., 1989).

With the goal to assess the role of ethnicity in determining the age of onset and severity of ALD and to compare the risk factors for progression of alcoholic fatty liver, alcoholic hepatitis, or alcoholic cirrhosis among ethnic groups, we conducted a retrospective chart review of all cases of ALD, that were admitted at University of California Davis Medical Center between 2002 and 2010 or were followed as outpatients in the same institution. We correlated clinical features and comorbidities with ethnicity with the final goal to identify risk factors and predictors of each of these stages of ALD.

Methods

This study was a single center retrospective chart review of 791 patients with ALD seen on an outpatient basis or hospitalized at the University of California Davis Medical Center in Sacramento, California between 2002-2010. 862 cases with ICD9 codes for ALD where

positively identified and 71 cases were excluded because they had no significant alcohol history, had other underlying diseases (HBsAb positivity, HIV positivity, and hemochromatosis, alpha 1 anti-trypsin deficiency, primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis), or were post- liver transplant. Patients with concomitant diagnoses of ALD and chronic hepatitis C were included given the high incidence of this viral infection in the United States Hispanic population with 1.5-2% of hepatitis C antibody positivity (Kuniholm et al., 2014). In addition, in order to account for this potential confounder, separate subgroup analyses were performed after exclusion of patients who were both HCV Ab and HCV RNA positive. The patients who met the inclusion criteria were further divided according to clinical presentation, laboratory data and imaging into the three diagnostic groups of alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis.

Alcoholic fatty liver was defined according to positive liver ultrasound criteria with normal serum laboratory tests or only mildly elevated AST and ALT (range 60-90 U/L) in an asymptomatic patient with history of chronic alcohol abuse. Since there were no liver biopsies in this group to distinguish those with additional fibrosis, all subjects with fatty liver according to ultrasound were included in this category. Alcoholic hepatitis was defined as at least one episode of jaundice and coagulopathy in a patient with alcohol abuse, leukocytosis (white blood cell count greater than 10,000/mm^3) or acute decompensation (new onset of ascites, jaundice and worsening coagulopathy) in a patient with known alcoholic cirrhosis and recent alcohol abuse where no other causes for decompensation were identified. The definition of alcoholic cirrhosis included clinical features of portal hypertension and/or end stage liver disease (thrombocytopenia, splenomegaly, esophageal or gastric varices, ascites and/or peripheral edema, hepatic encephalopathy, hepatorenal syndrome) in a patient with alcohol abuse. According to the United States Census 2006 American Community survey (www.census.gov/acs/www/), the Hispanic population in the Sacramento county includes about 80% of individuals with Mexican heritage.

We identified ethnicity, gender, age, abstinence status at presentation, drinking pattern as moderate or heavy, and laboratory data, (including serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), international normalized ratio (INR), and albumin, with AST to ALT ratio over 2 being highly suggestive of ALD (Rosman and Lieber, 1994, Salaspuro, 1986). Ethnicity was disclosed by the patient in the “Demographic section” of the Electronic Medical Record or else specified in physician or social worker notes. Other recorded data included imaging by abdominal ultrasound, computerized tomography (CT) scan or magnetic resonance imaging (MRI) for identification of hepatic architecture, hepatomegaly, steatosis, and signs of portal hypertension including splenomegaly, gastric or esophageal varices, and ascites, body mass index (BMI), presence or absence of metabolic syndrome, diabetes mellitus, chronic viral hepatitis C, other substance abuse, gastrointestinal bleeding, number of emergency room visits and hospitalizations for alcohol related morbidity. Metabolic syndrome was defined according to the 2006 International Diabetes Federation Criteria that include central obesity, raised serum triglyceride levels, hypertension, and increased fasting plasma glucose with reduced HDL-cholesterol (Alberti et al., 2005). Discriminant Function (calculated as 4.6 * (Pt's PT - Control PT) + TBili)

lower or higher than 32 was recorded as the index of severity in patients with alcoholic hepatitis (Maddrey et al., 1978).

Drinking patterns were defined by the following: moderate drinking as no more than 4 drinks a day or 14 drinks per week for men no more than 3 drinks per day, or 7 drinks per week for women and heavy drinking as 15 or more drinks per week, or four drinks in a day, for men or, more than seven drinks per week, or three drinks a day for women. Binge drinking was defined as consuming 5 or more drinks for male or 4 or more drinks in female in about 2 hours on multiple occasions. Our analyses did not include several substance abuse characteristics such as abstinence, beverage choice, or drinking duration, since no ethnicity differences were found in the frequency of these variables.

Statistical analyses

The age of presentation was compared between categories using analysis of variance (ANOVA). When the P-value for the overall F-test for the ANOVA model was significant, the age of presentation was compared pairwise between groups using the Tukey HSD (Honestly Significant Difference) method. A significant p-value from the Tukey HSD test indicates that the means between the two groups being compared are significantly different, even after adjusting for multiple testing.

Multiple regression models were selected using a forward and backwards-stepwise selection method, starting from the model with no covariates and using the Akaike Information Criterion (AIC), a commonly used model selection criterion, to select variables to enter and exit the model. P-values reported for categorical variables in multiple regression models are from non-sequential F-tests, followed by pairwise comparisons using the Tukey HSD method when an F-test was significant.

Categorical variables were compared between ethnic groups using Fisher's exact test where computationally feasible and using chi-square tests otherwise. Continuous variables were compared between ethnic groups using ANOVA.

Results

From 2002 to 2010, 791 patients were identified with the clinical diagnosis of ALD, including alcoholic fatty liver (16.4 %), alcoholic hepatitis (19.4 %), or alcoholic cirrhosis (64%) according to our defined criteria. The alcoholic hepatitis category included those with additional clinical features of alcoholic cirrhosis, whereas those categorized as alcoholic cirrhosis alone did not have specific clinical features of active hepatitis.

General demographics

There were 791 total patients in our total analysis, including 130 with alcoholic fatty liver, 154 with alcoholic hepatitis, and 507 patients with alcoholic cirrhosis respectively (Table 1). The majority of our patients were male, comprising 71%, 64% and 70% of each of the diagnostic categories. There was a majority of White/Caucasian patients in all three disease categories. Of note, the percentage of White/Caucasian and Hispanic patients in our studied population was similar to their percentage in the general population of Sacramento County

(www.census.gov/acs/www/). Sixteen percent of the alcoholic cirrhotic patients were hepatitis C Ab and RNA positive, whereas 2-4% of subjects in the alcoholic fatty liver or alcoholic hepatitis categories were hepatitis C Ab and RNA positive. The mean age of presentation for alcoholic fatty liver was 48.3 years, 46 years in patients with alcoholic hepatitis, and 52 years in alcoholic cirrhosis (Table 2). Hispanic patients presented in each of the three disease severity categories at significantly 4-10 years younger ages than the White/Caucasian patients. Hispanic cirrhotics also presented on average at 5 years younger age than African/American patients. In each of the three severity categories of ALD, the numbers of male patients were significantly greater among Hispanics compared to all other ethnicities (Table 3). When excluding subjects with metabolic syndrome, Hispanic patients with fatty liver or cirrhosis were still younger than White/Caucasian patients ($p=0.01$ for both categories), whereas there were no ethnicity differences in the age of patients with alcoholic hepatitis. When including in the analysis only subjects HCV Ab positive and RNA negative pooled with HCV Ab negative subjects, Hispanics subjects were younger than White/Caucasian in all three disease categories ($p<0.02$).

Multiple regression analyses were performed on all data, using a stepwise model selection that included unique variables for each form of alcoholic liver disease. For alcoholic fatty liver, the stepwise selection procedure only selected ethnicity as best predictive of age of presentation. In this model (as previously mentioned) Hispanic patients had a significantly earlier age of presentation than White/Caucasian patients and African/American patients. These differences remained significant after excluding patients with the metabolic syndrome ($p = 0.190$ for Hispanic vs. White/Caucasian and $p = 0.036$ for Hispanic vs. African/American) and excluding patients who were HCV Ab and RNA positive ($p = 0.002$ for Hispanic vs. White/Caucasian, $p = 0.021$ for Hispanic vs. African/American). For alcoholic hepatitis, a regression analysis was performed using metabolic syndrome, ethnicity, BMI, and imaging. When controlling for the other variables in the model, Hispanic patients had a significantly earlier age of presentation than White/Caucasian patients (Tukey HSD $p = 0.016$), and African/American patients had a significantly earlier age of presentation than White/Caucasian subjects ($p = 0.008$) and subjects of other race. When including only subjects without metabolic syndrome, no significant differences were seen among ethnicities. Among subjects with alcoholic hepatitis and HCV Ab positive and RNA negative pooled with HCV Ab negative, Hispanics had a significantly younger age of presentation than White/Caucasian ($p=0.018$). For alcoholic cirrhosis, a regression analysis was performed using ethnicity, duration of drinking, laboratory values, substance abuse, GI bleed, emergency room (ER) visits, and imaging as best fitting the age of presentation. When controlling for the other variables, ethnicity was not significantly associated with age of presentation. However, when excluding subjects with metabolic syndrome from the analysis, Hispanic subjects had a significantly younger age of presentation than White/Caucasian subjects (Tukey HSD $p = 0.001$) and African/American subjects (Tukey HSD $p = 0.013$). When excluding subjects with alcoholic cirrhosis who were and HCV Ab positive and HCV RNA positive, Hispanic subjects likewise had a significantly younger age of presentation than White/Caucasian subjects (Tukey HSD $p < 0.001$) and African/American subjects (Tukey HSD $p = 0.023$).

Co-morbidities by Ethnicity

African/American patients with alcoholic hepatitis were more likely to present with positive HCV RNA than White/Caucasian (Table 4). Hispanic patients in all three categories were more likely to be obese than White/Caucasians. There were fewer Hispanic patients with normal BMI and more obese Hispanic patients than would be expected if the underlying proportions in each BMI category were equal between ethnic groups (chi-square test $p < 0.001$) (Table 5). Hispanic cirrhotics were more likely to be diabetic and suffer from the entire clinical spectrum of the metabolic syndrome than African/American or White/Caucasian patients; however this difference was not seen in patients with alcoholic fatty liver or alcoholic hepatitis (Tables 6 and 7). Among patients with alcoholic hepatitis, the proportion of subjects with severe alcoholic hepatitis, as indicated by DF>32, was similar in Hispanic and White/Caucasian patients, but lower in African/American subjects.

There was significant variability by ethnicity in regards to the pattern of drinking. A significantly lower proportion of White/Caucasian subjects were binge drinkers compared to Hispanic subjects ($p = 0.040$) and AA subjects ($p = 0.007$) (Table 9).

Number of Hospitalizations and ER visits

There were significant differences among ethnicities for both numbers of hospitalization and numbers of ER visits for all three types of alcoholic liver disease. African/American patients with alcoholic fatty liver and alcoholic hepatitis averaged 6.3 and 3.5 times more hospitalizations and 4.3 and 7.5 times more ER visits than White/Caucasian patients in each disease category. White/Caucasian cirrhotic patients averaged fewer hospitalizations or ER visits as compared to Hispanic patients (Table 10) and the difference was still significant after excluding patients HCV Ab positive and HCV RNA positive from the analysis.

Discussion

The major findings of our study relate to the clinical differences in the incidence and expression of ALD among common ethnicities in the area of Sacramento, California, particularly between the Hispanic population when compared to Caucasians and African/Americans. First, we found that Hispanic patients presented with ALD at a significantly earlier age than Caucasians and African/Americans, and ethnicity was a predictor of age at presentation in alcoholic fatty liver and alcoholic hepatitis. Second, Hispanic patients with ALD were more likely to be obese when compared with White/Caucasians. Third, we found that Hispanic patients with alcoholic hepatitis or cirrhosis were more likely to be male than White/Caucasians. Fourth, Hispanic cirrhotic patients were also more likely to be diabetic and suffer from other features of the metabolic syndrome than other ethnicities. Fifth, African/Americans with alcoholic hepatitis were more likely to present with hepatitis C than other ethnicities. Finally, we found that Hispanic or African/American cirrhotics were more likely to be hospitalized than Caucasian cirrhotics.

While it has been shown that alcoholic cirrhosis is a major public health issue in the Hispanic community, few studies have examined the features and epidemiology of all three stages of ALD in this population. Flores et al examined the prevalence of specific risk

factors including elevated serum aminotransferase activity, hepatitis B or C infection, heavy or binge drinking, obesity, diabetes, and metabolic syndrome in White/Caucasian, African/American and Mexican/American chronic liver disease populations in the United States and found that Mexican/Americans were most likely to have elevated serum aminotransferase levels, while Mexican/American men were more likely to be obese than Mexican American women (Flores et al., 2008). In their description of African/Americans with chronic liver disease as well as ours, we each found that African/Americans are more likely to be co-infected with hepatitis C. Most of the published literature on this point has focused on the relatively high prevalence and increased mortality of ALD in Hispanic alcoholic cirrhotics. Using the Nationwide Inpatient Sample, Yang et al. showed that alcoholic cirrhosis was more prevalent in the U.S. Hispanic community than in the Caucasian or African/American populations, with 16.9 cases per 100,000 vs 11.1 and 9.9 respectively (Yang et al., 2008). This finding was thought to be related to ethnic variations in drinking habits. However, while our data shows a higher percentage of binge drinking in our Hispanic population, there was not a significant difference in our percentage of Hispanic heavy drinkers when compared to the Caucasian population. Singh et al. also focused on alcoholic cirrhosis mortality and showed that, when controlling for age, place of birth, marital status, place of residence, education, occupation and family income, Hispanic American men were more likely to die of alcoholic cirrhosis than both White Caucasian or African/American patients (Singh and Hoyert, 2000). Finally, Yoon et al. showed that the annual average age-adjusted death rate from all liver cirrhosis was higher for Hispanics as a whole than for non-Hispanic White/Caucasians (Yoon et al., 2011).

Whereas there have been several reports regarding ethnic differences in the incidence of alcoholic cirrhosis, much less has been published on differences in incidences of alcoholic hepatitis and alcoholic fatty liver disease. Browning et al examined hepatic steatosis regardless of etiology (alcoholic and non-alcoholic fatty liver) and found a significant variation in its prevalence across ethnicities (Browning et al., 2004). The cause of this variation was unclear, as both Hispanic and African/Americans were more likely to be insulin resistant and obese, which are known risk factors for hepatic steatosis (Loomba and Sanyal, 2013). However while Hispanics had a higher prevalence of alcoholic fatty liver than expected, in African/Americans it was lower.

There are several potential reasons for the earlier age of presentations of alcoholic fatty liver disease and alcoholic hepatitis in Hispanics. Regarding alcoholic fatty liver, known risk factors of obesity and diabetes have been shown to be more prevalent in young Hispanics when compared to non-Hispanic whites (Harris et al., 1998) (Escarce JJ, 2006). Interestingly, when excluding subjects with metabolic syndrome from the analysis, Hispanics patients with alcoholic fatty liver or cirrhosis were still younger than White/Caucasian patients, whereas age of presentation in case of alcoholic hepatitis was affected by the presence of metabolic syndrome. Therefore, metabolic syndrome and its associated comorbidities is a factor potentially contributing to earlier age of presentation primarily in case of alcoholic hepatitis. Genetic factors have also been studied. The rs738409 variant of patatin-like phospholipase domain-containing protein 3 (*PNPLA3*) has been determined by genome-wide associated studies to associate with hepatic fat content and markers of

hepatocyte damage, thought to be due to its role in hepatic fat storage (Romeo et al., 2008, Yuan et al., 2008). Tian et al showed that the rs738409[G] allele in *PNPLA3* was strongly associated with ALD, and, since this allele is more common in Hispanics with a greater genetic predisposition to fatty liver disease, it may also account for greater incidences of both non-alcoholic and alcoholic steatosis (Tian et al., 2010, Romeo et al., 2008). The methylenetetrahydrofolate reductase enzyme (MTHFR) has also been studied due to its role in folate and methionine metabolism (Chiuve et al., 2005), an area with which alcohol is known to interfere (Halsted and Medici, 2011)

MTHFR variants have been described in chronic alcoholic patients in association with the development of colon cancer, hepatocellular carcinoma, and alcoholic cirrhosis, (CC vs TT haplotypes) (Saffroy et al., 2004, Fabris et al., 2009). While distributed heterogeneously worldwide, it is important to note that the MTHFR 677TT genotype occurs with the highest frequency in Mexico compared to other countries where it has been quantified (Gueant-Rodriguez et al., 2006)

Other active areas of research have focused on potential genetic differences in ethanol metabolism. Alcohol dehydrogenase 1B (ADH1B), aldehyde dehydrogenase 2 (ALDH2), and Cytochrome P450 (CYP2E1) have all been studied, with the most promising data arising from study of the latter. Khan et al found that the cytochrome P450 2E1 (CYP2E1)*5B variant genotype was associated with an increased risk of alcoholic cirrhosis when compared to alcoholic patients without signs of liver disease in an Indian population (Khan et al., 2009). Zeng et al performed a meta-analysis investigating the role of CYP2E1 polymorphisms in ALD and, while there were no significant associations with alcoholic cirrhosis, their findings suggested that the Pst I/Rsa I polymorphism might be associated with alcoholic fatty liver and hepatitis (Zeng et al., 2013). Finally, García-Bañuelos et al showed a significant increase in the presence of the CYP2E1 c2 allele in cirrhotics from Western Mexico (Garcia-Banuelos et al., 2012). Comparing ethnicities, the CYP2E1*c2 allele has been shown to occur with high frequency in Mexican-Americans when compared to Europeans (Gordillo-Bastidas et al., 2010).

There are several limitations in interpretation of the results of our study. Primarily, our sample size is relatively small in our single center study, particularly among our population of alcoholic hepatitis and alcoholic fatty liver patients. Accordingly, a wide variety of ethnicities had to be placed in the Other group that included Asian of various origins, Middle Eastern, Native American and Alaskan Native.

While our center is the only academic medical center in one of the America's most ethnically diverse cities, we did not accumulate enough cases over our specified review period to examine each of these minorities separately. The hepatitis C population may be worth additional study, since alcohol has been shown to increase liver disease progression in hepatitis C (Ostapowicz et al., 1998). However, the exclusion of subjects positive for active hepatitis C did not change the main results regarding age at presentation or number of hospitalizations. We encountered the same limitations as other retrospective chart review studies. We were reliant on information in the medical record without an appropriate way to verify or acquire information that was not originally collected. Another limitation of our

study was our reliance on self-reporting of alcohol use as this information tends to be under-reported. Future studies may benefit from larger databases that may have the capability to classify patients by more specific ethnicity.

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Table 1

Cumulative Patient Data (n, %)

	Alcoholic Fatty Liver	Alcoholic Hepatitis	Alcoholic Cirrhosis	Total patients included in the analysis
Total Patients	130	154	507	
Male Gender	86 (66)	95 (62)	345 (68)	791
Ethnicity				
White/Caucasian	81 (62)	101 (66)	311 (61)	493 (62)
Hispanic	18 (14)	28 (18)	113 (22)	159 (20)
African/American	9 (7)	11 (7)	30 (6)	50 (6)
Other	22 (17)	14 (9)	53 (10)	89 (11)
Co-Morbidities				
HBV Core Ab Positive	0	1 (1)	4 (1)	
HCV Ab Positive, HCV RNA positive	5 (4)	4 (3)	80 (16)	89 (11)
HCV Ab Positive and HCV RNA Negative or HCV Ab Negative	86 (67)	135 (88)	346 (68)	567 (72)
HCV status unknown	48 (36)	8 (7)	79 (16)	135 (18)
Type 2 Diabetes Mellitus	20 (15)	16 (10)	109 (21)	
Metabolic Syndrome	59 (45)	21 (14)	128 (25)	

Table 2

Age of Presentation (Mean Age, SD)

	Alcoholic Fatty Liver	Alcoholic Hepatitis	Alcoholic Cirrhosis
Mean	48.3	46	52
White/Caucasian	51 (10)[a]	47 (9)[a]	53 (9)[a]
Hispanic	41 (8)[b]	41 (8)[b]	49 (9)[b]
African/American	53 (7)[a]	48 (9)	54 (8)[a]
Other	43 (13)[b]	47 (10)	50 (10)

Different letters in the vertical columns indicate significant p values (<0.05) within the same clinical entity (alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis). This table and the following tables exclude HIV, HBsAg positive, and HCV RNA positive patients.

Alcoholic Fatty liver: Hispanic significantly younger age than White/Caucasian ($p = 0.002$) and AA, other significantly younger than White/Caucasian ($p = 0.009$)

Alcoholic Hepatitis: Hispanics significantly younger than White/Caucasian ($p=0.012$)

Alcoholic Cirrhosis: Hispanics significantly younger age than White/Caucasian ($p = 0.001$) and AA ($p = 0.006$).

Table 3

ALD Type by Sex and Ethnicity (%)

ALD Type	Sex	White/Caucasian	Hispanic	AA	Other	P-Value
Alcoholic	F	39	17	67	18	0.019
Fatty Liver	M	61	83[a]	33[b]	82[a]	
Alcoholic	F	46	14	45	29	0.013
Hepatitis	M	54[a]	86[b]	55	71	
Alcoholic	F	39	17	37	21	<0.001
Cirrhosis	M	61[a]	83[b]	63[b]	79[b]	

P-value (Fisher's exact test) indicates the proportion of male patients differs significantly by ethnicity. Different letters reading horizontally indicate significant p values (<0.05) within the same clinical entity.

Alcoholic fatty liver: Hispanic vs. AA, p = 0.026; AA vs. other, p = 0.015; White/Caucasian vs. Hispanic p= 0.101.

Alcoholic hepatitis: White/Caucasian vs. Hispanic, p= 0.002.

Alcoholic Cirrhosis: White/Caucasian vs. Hispanic p < 0.001, White/Caucasian vs. other p = 0.018, Hispanic vs. AA p = 0.042

Table 4

Hepatitis C by Ethnicity (n,%)

	White/Caucasian	Hispanic	AA	Other P-Value
Alcoholic Fatty Liver				0.065
HCV Ab positive/RNA positive	3 (4)	0	2 (22)	0
Alcoholic Hepatitis				0.044
HCV Ab positive/RNA positive	2 (2)[a]	0	2 (18)[b]	0
Alcoholic Cirrhosis				0.155
HCV Ab positive/RNA positive	51 (16)	15 (13)	8 (27)	6 (11)

P-value (Fisher's exact test) indicates that the proportion of Hepatitis C RNA positive patients differs significantly in the Alcoholic Hepatitis group. Different letters horizontally indicate significant p values (<0.05) within each clinical entity.

Alcoholic hepatitis: the proportion of HCV RNA positive subjects is significantly higher for AA subjects than White/Caucasian subjects (p = 0.044).

Table 5

Body Mass Index by Ethnicity (n,%)

	White/Caucasian	Hispanic	AA	Other P-Value
Alcoholic Fatty Liver				0.019
Underweight <18.5	2 (3)	0	0	2 (9)
Normal 18.5-24.9	20 (25)	2 (11)	4 (44)	4 (18)
Overweight 25-29.9	30 (38)	1 (6)	2 (22)	10 (45)
Obese >30	25 (31)[a]	12 (67)[b]	3 (33)	5 (23)[a]
Alcoholic Hepatitis				0.003
Underweight <18.5	4 (4)	0	1 (9)	0
Normal 18.5-24.9	45 (45)	10 (36)	4 (36)	11 (79)
Overweight 25-29.9	31 (31)	6 (21)	2 (18)	3 (21)
Obese >30	20 (20)[a]	12 (43)[b]	3 (27)	0[a]
Alcoholic Cirrhosis				<0.001
Underweight <18.5	7 (2)	0	2 (7)	1 (2)
Normal 18.5-24.9	126 (41)	14 (13)	10 (33)	21 (40)
Overweight 25-29.9	90 (30)	42 (38)	11 (37)	18 (35)
Obese >30 kg/m2	77 (25)[a]	51 (46)[b]	6 (20)[a]	10 (19)[a]

P-value (chi-square test) indicates the distribution of patients among BMI categories differing significantly between ethnicities. Different letters horizontally indicate significant p values (<0.05) within the same clinical entity.

Alcoholic Fatty liver: the proportion of obese subjects is significantly higher for Hispanic subjects than White/Caucasian subjects ($p = 0.002$) and subjects of other race ($p = 0.003$). BMI data is missing for 17% of Hispanic subjects with alcoholic fatty liver disease

Alcoholic hepatitis: the proportion of obese subjects is significantly higher for Hispanic subjects than White/Caucasian subjects ($p = 0.026$) and subjects of other race ($p = 0.011$).

Alcoholic Cirrhosis: The proportion of obese subjects is significantly higher in Hispanic subjects than White/Caucasian subject ($p < 0.001$), AA subjects ($p = 0.016$), and subjects of other race ($p = 0.002$).

Table 6

Diabetes Mellitus Type 2 by Ethnicity (n,%)

	White/Caucasian	Hispanic	AA	Other P-Value
Alcoholic Fatty Liver				0.446
No	69 (86)	16 (89)	6 (67)	19 (86)
Yes	11 (14)	2 (11)	3 (33)	3 (14)
Alcoholic Hepatitis				0.040
No	90 (90)	26 (93)	7 (64)	14 (100)
Yes	10 (10)	2 (7)	4 (36)	0
Alcoholic Cirrhosis				0.001
No	251 (83)	71 (65)	26 (87)	40 (77)
Yes	53 (17)[a]	39 (35)[b]	4 (13)	12 (23)

P-value (Fisher's exact test) indicate the proportion of patients with DM differs significantly by ethnicity. Different letters horizontally indicate significant p values (<0.05) within the same clinical entity.

Alcoholic hepatitis: rates of DM are significantly higher in AA subjects than in White/Caucasian subjects ($p = 0.032$), Hispanic subjects ($p = 0.042$), and subjects of other race ($p = 0.026$).

Alcoholic Cirrhosis: rates of DM are significantly higher in Hispanic subjects than in White/Caucasian subjects ($p < 0.001$) and AA subjects ($p = 0.025$).

Table 7

Metabolic Syndrome by Ethnicity (n,%)

	White/Caucasian	Hispanic	AA	Other	P-Value
Alcoholic Fatty Liver					0.490
No	42 (53)	11 (61)	7 (78)	11 (50)	
Yes	38 (48)	7 (39)	2 (22)	11 (50)	
Alcoholic Hepatitis					0.219
No	85 (85)	25 (89)	8 (73)	14 (100)	
Yes	15 (15)	3 (11)	3 (27)	0	
Alcoholic Cirrhosis					0.013
No	239 (76)	69 (60)	24 (77)	39 (76)	
Yes	65 (24)[a]	41(40)[b]	6 (23)	13 (24)	

P-values (Fisher's exact test) indicate the proportion of patients with metabolic syndrome differs significantly among ethnicities. Different letters horizontally indicate significant p values (<0.05) within the same clinical entity.

Alcoholic Cirrhosis: rates of metabolic syndrome are significantly higher in Hispanic subjects than in White/Caucasian subjects (p = 0.001).

Table 8

Discriminant Factor by Ethnicity (n,%)

Discriminant Function	White/Caucasian	Hispanic	AA	Other	P-Value
<32 (n, %)	58 (61)	12 (43)	11 (100)	5 (36)	0.001
>32 (n, %)	37(39)[b]	16 (57)[b]	0 (0)[a]	9 (64)[b]	

P-value (Fisher's exact test) indicates the proportion of patients with DF >32 differs significantly by ethnicity. Different letters horizontally indicate significant p values (<0.05) within the same clinical entity.

The proportion of subjects with DF > 32 is significantly lower for AA subjects than for White/Caucasian (p = 0.008), Hispanic (p = 0.001), or other race subjects (p = 0.001)

Maddrey Discriminant Function (DF) is defined as DF = (4.6 × [prothrombin time (sec) - control prothrombin time (sec)]) + (serum bilirubin in mg/dL) (Maddrey et al., 1978)

Table 9

Pattern of Drinking by Ethnicity (n,%)

	White/Caucasian	Hispanic	AA	Other	P-Value
Alcoholic Fatty Liver					0.193
Low Risk	3 (4)	0	0	0	
Moderate drinking	10 (14)	6 (46)	1 (13)	6 (33)	
Heavy drinking	45 (64)	5 (38)	4 (50)	8 (44)	
Binge drinking	12 (17)	2 (15)	3 (38)	4 (22)	
Alcoholic Hepatitis					0.801
Moderate drinking	6 (6)	0	1 (11)	1 (7)	
Heavy drinking	74 (79)	25 (89)	7 (78)	11 (79)	
Binge drinking	15 (16)	3 (11)	1 (11)	2 (14)	
Alcoholic Cirrhosis					0.025
Moderate drinking	22 (8)	5 (5)	3 (12)	5 (10)	
Heavy drinking	266 (91)	95 (90)	20 (77)	44 (88)	
Binge drinking	4 (1)[a]	6 (6)[b]	3 (12)[b]	1 (2)	

P-value (chi-square test) indicates the distribution of patients among drinking pattern categories differs significantly by ethnicity. Different letters horizontally indicate significant p values (<0.05) within the same clinical entity.

Alcoholic cirrhosis: a significantly lower proportion of White/Caucasian subjects were binge drinkers compared to Hispanic subjects (p = 0.040) and AA subjects (p = 0.007).

Table 10

Hospitalizations and ER Visits by Ethnicity

Alcoholic Fatty Liver	W/C	Hispanic	AA	Other	P-Value
Hospitalizations					0.010
Mean (SD)	0.3 (0.8)[a]	0.3 (0.8)[a]	1.9 (4.1)[b]	0.4 (0.8)[a]	
Median (Range)	0 (0-5)	0 (0-3)	0 (0-12)	0 (0-3)	
ER visits					0.014
Mean (SD)	0.7 (1.8)[a]	1.8 (3.5)	3.4 (4.6)[b]	0.9 (2.7)	
Median (Range)	0 (0-10)	0 (0-11)	0 (0-10)	0 (0-10)	

Alcoholic Hepatitis	W/C	Hispanic	AA	Other	P-Value
Hospitalizations					<0.001
Mean (SD)	1.4 (1.7)[a]	1.6 (1.4)[a]	4.9 (4.0)[b]	2.3 (2.2)[a]	
Median (Range)	1 (0-10)	1 (0-5)	4 (1-12)	2 (0-8)	
ER visits					<0.001
Mean (SD)	0.9 (2.2)[a]	2.2 (2.6)[a]	6.8 (4.1)[b]	2.2 (2.6)[a]	
Median (Range)	0 (0-17)	2 (0.0-11.0)	8 (0-12)	1 (0-8)	

Alcoholic Cirrhosis	W/C	Hispanic	AA	Other	P-Value
Hospitalizations					<0.001
Mean (SD)	1.4 (2.2)[a]	2.5 (3.1)[b]	1.9 (2.3)	2.3(3.6)	
Median (Range)	0 (0-11)	1 (0-13)	1 (0-12)	1 (0-17)	
ER visits					<0.001
Mean (SD)	1.0 (2.3)[a]	2.0 (3.5)[b]	2.4 (4.0)[b]	2.3 (4.0)[b]	
Median (Range)	0 (0-17)	0 (0-17)	0 (0-12)	0 (0-20)	

P-value from ANOVA F-test. W/C: White/Caucasian. AA: African/American. Different letters indicate significant p values (<0.05) within the same clinical entity (alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis).

Alcoholic fatty liver: AA subjects had significantly more hospitalizations than White/Caucasian ($p = 0.005$), Hispanic ($p = 0.022$), and other race subjects ($p = 0.026$). AA subjects had significantly more ER visits than White/Caucasian subjects ($p = 0.011$).

Alcoholic hepatitis: AA subjects had significantly more hospitalizations than White/Caucasian ($p < 0.001$), Hispanic ($p < 0.001$), and other race subjects ($p = 0.005$). AA subjects also had significantly more ER visits than any other group ($p < 0.001$ for all comparisons).

Alcoholic cirrhosis: number of hospitalizations was significantly higher in Hispanic subjects than in White/Caucasian subjects ($p < 0.001$). Number of ER visits was significantly lower in White/Caucasian subjects than in Hispanic subjects ($p = 0.007$), AA subjects ($p = 0.006$), and subjects of other race ($p = 0.011$).